



1           5.    The method of claim 3, wherein the vessel is  
2 maintained at a constant temperature as the pressure is  
3 cycled.

1           6.    The method of claim 1, further comprising  
2 washing away unhybridized nucleic acids after increasing the  
3 pressure but before decreasing the pressure.

1           7.    The method of claim 1, wherein the pressure  
2 inside the vessel is increased to greater than 10,000 psi.

1           8.    A method of detecting in a sample the presence  
2 of a nucleic acid that hybridizes to a reference nucleic  
3 acid at a first higher pressure but not at a second lower  
4 pressure, the method comprising:

5           (1)   providing a sample vessel and pressure  
6 controller for the vessel; and in any order

7           (2)   contacting the reference sequence with the  
8 sample in the vessel at the first pressure;

9           (3)   contacting the reference sequence with the  
10 sample in the pressure vessel at the second pressure; and

11           (4)   detecting the presence of a nucleic acid that  
12 hybridizes to the reference nucleic acid at the first  
13 pressure but not at the second pressure.

1           9.    The method of claim 8, wherein the reference  
2 sequence is first contacted with the sample and  
3 hybridization is detected, and then the pressure is lowered  
4 and the absence of hybridization is detected.

10. A method of discriminating between a first nucleic acid and a second nucleic acid that is different from the first nucleic acid, the method comprising,

(1) providing a sample vessel and pressure controller for the vessel;

(2) maintaining the vessel at a constant pressure;

(3) providing the first and second nucleic acid and a reference nucleic acid in the vessel under conditions that do not allow either the first or the second nucleic acid to hybridize to the reference nucleic acid;

(4) perturbing at least one condition to establish conditions that permit the first nucleic acid to form a complex with the reference nucleic acid at equilibrium and to permit the second nucleic acid to form a complex with the reference nucleic acid at equilibrium; and

(5) comparing the time necessary to achieve equilibrium hybridization between the first nucleic acid and the reference nucleic acid with the time necessary to achieve equilibrium hybridization between the second nucleic acid and the reference nucleic acid, wherein the difference indicates the relative difference in sequence between the first and the second nucleic acids.

11. The method of claim 10, wherein the perturbation is a change in temperature inside the vessel.

12. The method of claim 10, wherein the perturbation is a change in an electric field inside the vessel.

13. The method of claim 10, wherein the sample vessel is maintained at a pressure of at least 10,000 psi.

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1 14. A method of discriminating between a first  
2 nucleic acid and a second nucleic acid that is different  
3 from the first nucleic acid, the method comprising,  
4 (1) providing a sample vessel and pressure  
5 controller for the vessel;  
6 (2) providing the first and second nucleic acid and  
7 a reference nucleic acid in the vessel under a first  
8 pressure that does not allow either the first or the second  
9 nucleic acid to hybridize to the reference nucleic acid;  
10 (3) perturbing the pressure to establish conditions  
11 that permit the first nucleic acid to form a complex with  
12 the reference nucleic acid at equilibrium and to permit the  
13 second nucleic acid to form a complex with the reference  
14 nucleic acid at equilibrium; and  
15 (4) comparing the time necessary to achieve  
16 equilibrium hybridization between the first nucleic acid and  
17 the reference nucleic acid with the time necessary to  
18 achieve equilibrium hybridization between the second nucleic  
19 acid and the reference nucleic acid, wherein the difference  
20 indicates the relative difference in sequence between the  
21 first and the second nucleic acids.

1 15. The method of claim 14, wherein the sample  
2 vessel is maintained at a pressure of at least 10,000 psi.

1 16. The method of claim 4, wherein a portion of the  
2 second nucleic acid is amplified.